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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/884,526	06/19/2001	David Meeker	07680.0019.00000	2532

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EXAMINER	
CHEN, SHIN LIN	
ART UNIT	**PAPER NUMBER**
1632	

DATE MAILED: 06/10/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action	Application No.	Applicant(s)	
	09/884,526	MEEKER ET AL.	
	Examiner	Art Unit	
	Shin-Lin Chen	1632	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 17 May 2004 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.

b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☐ A Notice of Appeal was filed on _____. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.
2. ☐ The proposed amendment(s) will not be entered because:
   (a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ they raise the issue of new matter (see Note below);
   (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.
   NOTE: _____.
3. ☒ Applicant's reply has overcome the following rejection(s): See Continuation Sheet.
4. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
5. ☒ The a)☐ affidavit, b)☐ exhibit, or c)☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: *See Continuation Sheet*.
6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.
7. ☒ For purposes of Appeal, the proposed amendment(s) a)☐ will not be entered or b)☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

   The status of the claim(s) is (or will be) as follows:

   Claim(s) allowed: *None*.

   Claim(s) objected to: *None*.

   Claim(s) rejected: *1 and 4-6*.

   Claim(s) withdrawn from consideration: *2, 3 and 7-12*.
8. ☐ The drawing correction filed on _____ is a)☐ approved or b)☐ disapproved by the Examiner.
9. ☐ Note the attached Information Disclosure Statement(s)(PTO-1449) Paper No(s). _____.
10. ☐ Other: _____

S Chen

Shin-Lin Chen
Primary Examiner
Art Unit: 1632

Continuation of 3. Applicant's reply has overcome the following rejection(s): 35 U.S.C. 112 second paragraph rejection and 35 U.S.C. 11 rst paragraph new matter rejection.

Continuation of 5. does NOT place the application in condition for allowance because: Applicants argue that the unpredictability of gene herapy and enzyme therapy cited by examiner does not apply to Fabry disease. Applicants cite US Patent 6,066,626 and argue that a ector expressing human alpha-galactosidase A can be administered to an individual and reduce globotriaosylceramide (GL3) level in aid individual, wherein GL3 level is a known measuring stick for the efficacy of Fabry disease therapies. Applicants cite US Patent ,658,567 and further argue that enzyme replacement therapy was not unpredictable at the time of the invention (amendment, p. 7-8). his is not found persuasive because of the reasons of record. As discussed in the previous Official actions, the existence of animal nodel for Fabry disease does not warrant successful combination therapy of gene therapy and enzyme replacement therapy for Fabry isease. Although the assay method for monitoring the efficiency of the combination therapy was known in the art, however, the state of he art of gene therapy and enzyme replacement therapy were unpredictable at the time of the invention. The cited references provide upport for the conclusion that the state of gene therapy in vivo and enzyme replacement therapy in vivo were unpredictable at the time o ne invention and this also applies to the treatment of Fabry disease. US Patent 6,066,626 only reports a method of providing biologicall ctive human alpha-galactosidase A to cells of an individual by administering a vector expressing alpha-galactosidase A to said individua nd shows reduction of GL3 level in said individual. Delivering a human alpha-galactosidase A to cells of an individual and reduction of GL3 in the cells do not mean that the Fabry disease has been treated. The term "treating" implies that therapeutic effect would be btained and the symptoms of the Fabry disease are ameliorated. Reduction of GL3 level is only an indication of biochemical change. ncrease of GL3 level in a subject could be just a starting point of a series of events that result in Fabry disease having various symptoms herefore, reduction of GL3 level does not mean the symptoms of Fabry disease would be ameliorated, i.e. the Fabry disease is treated. here is also no evidence of record as to what extent the GL3 level is reduced would the Fabry disease symptoms be ameliorated. On th ther hand, patent 5,658,567 only teaches production of a recombinant human alpha-galactosidase A and suggests said alpha- alactosidase A can be used in enzyme replacement therapy to treat Fabry patients. Patent '567 fails to provide adequate guidance and vidence for how to treat Fabry disease in vivo with any vector expressing alpha-galactosidase A via various administration rotues. The rt of enzyme replacement therapy in vivo was unpredictable at the time of the invention. The administration route of the protein or nzyme, the amount of the protein or enzyme that reach the target cells, the stability of said protein or enzyme within the cells or during he process of administration, and the protein=s compartmentalization within the cell are all important factors for a successful enzyme eplacement therapy. Applicnats argue that the Office has provided no evidence to support the definition of the term :treating" and eiterates the teaching of patent '626 and measuring GL3 level is an accepted method for evaluating therapy for the disease (amendment . 9-10). This is not found persuasive because of the reasons of record and the reasons set forth above. The term "treatment" means th nedical or surgical management intended to ameliorate basic disease problems (see Stedman's medical dictionary 27th edition). It was vell known in the art that the term "treating" implies theraptuic effect in vivo and amelioration of disease symptoms. Thus, the claims emain rejected under 35 U.S.C. 112 first paragraph .